ALTERATION OF P53 ISOFORM EXPRESSION TO TREAT AGE-RELATED DISORDERS AND CANCER

SUMMARY

The National Cancer Institute seeks parties to co-develop or license a new method for inhibiting aging-related degenerative disease and cancer.

REFERENCE NUMBER

E-033-2008

PRODUCT TYPE

- Therapeutics

KEYWORDS

- age-related disorders
- p53
- Isoforms
- siRNA
- shRNA
- enhanced expression

COLLABORATION OPPORTUNITY

This invention is available for licensing.

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DESCRIPTION OF TECHNOLOGY

The protein p53 is encoded by the TP53 gene in humans. The p53 protein is crucial in multicellular organisms, where it regulates the cell cycle and, thus, functions as a tumor suppressor, preventing cancer. It plays a critical role in carcinogenesis and aging as evidenced by the occurrence of p53 mutations or p53 regulating proteins in over 50% of all cancers. Thus, intense efforts have been devoted to finding therapeutics capable of targeting and altering the p53 pathway.

Researchers at the NCI Laboratory of Molecular Genetics and Carcinogenesis discovered two isoforms of p53, D133p53 and p53b, capable of controlling p53 dependent carcinogenesis. The researchers also devised two distinct methods to either induce or circumvent p53-dependent cellular senescence as an

anti-proliferative chemotherapy or to treat aging-related degenerative disease, respectively. The interplay between two recently discovered isoforms of p53, D133p53 and p53b, are capable of controlling p53 mediated carcinogenesis. Anti-proliferation activity can be induced by siRNA and shRNA vectors to knock-down a naturally occurring inhibitor of p53-dependent cell senescence (D133p53), and/or increasing expression of p53b. Alternatively, the inventors have developed expression vectors capable of increasing intracellular levels of D133p53, leading to an extended cellular life cycle.

POTENTIAL COMMERCIAL APPLICATIONS

- Method to treat cancer, aging-related disorders, and promote tissue regeneration
- Pharmaceutical compositions to inhibit cancer or promote cell regeneration

COMPETITIVE ADVANTAGES

- Ability to treat a wide variety of cancers and age-related diseases, since the physiological p53 isoforms identified in this invention, as well as wild-type p53, are present in various types of normal cells
- Overexpression and shRNA therapeutics are stably integrated into the genome for long-term treatment

INVENTOR(S)

Curtis C Harris (NCI)

DEVELOPMENT STAGE

- Discovery (Lead Identification)

PUBLICATIONS

Tang T et al., PMID: 22777358;Fujita K et al., PMID: 19701195

PATENT STATUS

- **U.S. Issued:** 8,575,121
- **Foreign Filed:** CA 2705488, EU 08850046.7
- **Foreign Issued:** Australia Patent 2008321253

THERAPEUTIC AREA

- Cancer/Neoplasm